IN THE CLAIMS:

Please replace the text of claim 33 with the following text:

33. The method of claim 29, wherein the target biopolymer is a target polynucleotide, and the probe biopolymer is a polynucleotide that is complementary to the target polynucleotide.

Please replace the text of claim 35 with the following text:

35. The method of claim 34, wherein the biopolymer is a polynucleotide, the reporter is biotin, and the method of claim 34 further comprises a step of incubating the complex adsorbed on the surface of the polypropylene substrate with streptavidin-alkaline phosphatase and an ELF reagent for developing a fluorescent signal prior to the detecting step.

REMARKS:

Claims 1-54 are pending in the application. Claims 33 and 35 are amended. Reexamination and reconsideration of the application in view of the following remarks are respectfully requested.

The Examiner has required the restriction of further prosecution to one of the following inventions: a method of making an assay article for use in biopolymer detection, claims 1-28 (Group I); a method of detecting a target biopolymer, claims 29-42 (Group II); or an assay article and kit, claims 43-54 (Group III). In response, applicants hereby affirm the election of Group II, corresponding to claims 29-42, with traverse. Claims 29-42 are presented for further prosecution.

The Office Action states that the inventions of Groups II and III are distinct because the product as claimed can be used to practice another materially different process. The Examiner provides an example of "nucleic acid or protein purification" as such a materially different process.

Applicants submit, however, that the example given is not a process that is materially different from that claimed. The process referred to by the Examiner is one of the embodiments of the applicants' invention and it is covered, for example, by the broad language of the method claim 29. The terms "probe biopolymer" and

"target biopolymer" are broad terms including, *inter alia*, biopolymers present in a sample ("target biopolymers") that are purified from the sample by binding with the "probe biopolymers" adsorbed on the substrate. Moreover, the process referenced by the Examiner requires the same steps as the method inventions of Group II. The fact that the target biopolymer binds to the probe biopolymer for the purpose of purification rather than for the purpose of detection does not change the nature of the process.

The Examiner also appears to believe that the inventions of Groups II and III are distinct because the method of Group II can be used with other solid support detection, such as magnetic beads.

Applicants submit, however, that the example given is not a product that is materially different from that claimed. The product referred to by the Examiner (magnetic beads used as a solid support) is one of the embodiments of the applicants' invention and it is covered, for example, by the language of claim 44. Claim 44 recites, *inter alia*, beads as one of the types of the substrates that may be used in the present invention. Consequently, it is respectfully submitted that the method inventions of Group II are not distinct from the assay article and kit inventions of Group III.

The Office Action also states that the inventions of Groups I and III are distinct because the process as claimed can be used to make another materially different product, such as an affinity chromatography column.

Applicants submit, however, that the example given is not a product that is materially different from that claimed. The product referred to by the Examiner is one of the embodiments of the applicants' invention, which is covered, for example, by the broad language of the method claim 44. Claim 44 lists a wide range of substrates, including "foams, filaments, threads, sheets, films, slides, gels, membranes, beads, plates, and planar devices." Also, the specification emphasizes that the particular shape of the substrate is not crucial and "the substrates may be molded into any of a variety of shapes and forms" "in order to accommodate different testing techniques" (page 7, lines 23-31). Accordingly, even though the

present invention is particularly useful in the preparation of biopolymer arrays, the full scope of the invention is not limited to this particular embodiment and, thus, also covers affinity columns.

The Examiner also states that the inventions of Groups I and III are distinct because "claims 29-42 can be used to make the magnetic beads for biopolymer detection." However, since claims 29-42 do not belong to either Group I or Group III, applicants would like to receive a clarification from the Examiner on how the above-quoted statement is relevant to the restriction with respect to Groups I and III.

In addition, applicants respectfully submit that the literature searches required for Groups I, II, and III are not distinct from each other. A publication that deals with assay articles will usually disclose methods for making and using such an article. Therefore, because the art required to be searched for both invention groups is expected to be largely the same, applicant does not believe that there will be a serious burden on the Examiner if restriction is not required.

In light of the foregoing comments, it is requested that all of the claims be retained in a single case. In the event that the Office maintains its position with respect to restriction, however, applicants confirm their provisional election to prosecute in this application claims 29-42 (Group II) and reserves the right to file divisional applications directed to non-elected Group I (claims 1-28) and Group III (claims 43-54).

The Examiner objected to the title of the invention as not descriptive because it is directed to the immobilization of biopolymers on substrates, while the claims of Group II are directed to a method of detecting a target biopolymer. As noted above, however, applicants believe that all of the claims should be retained in a single case. Because the immobilization of biopolymers to aminated substrates by direct adsorption is a key concept of the present invention, the originally submitted title is sufficiently descriptive. However, in the event that the Office maintains its position with respect to restriction, applicants suggest the following title: "Use of an Assay Article Formed by Adsorption of Biopolymers on a Surface of a Substrate in

Detection of Target Biopolymers." Applicants respectfully request an indication from the Examiner about the suitability of such a title.

The Examiner objected to the specification because of the misspelling in the term "complimentary" on page 12, line 2, of the specification and in the claims 33. In response, applicants amended the specification and claim 33 to correct this typographical error.

Claims 35-37 are rejected because claim 35 depends from both claims 34 and 29, but claims 29 and 34 are not referred to in the alternative. In response, applicants amended claim 35 to correct a typographical error and to clarify that claim 35 is dependent solely on claim 34.

Claims 29-31 and 38-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification. The Examiner appears to believe that because generally the term "biopolymer" encompasses carbohydrates and fatty acids in addition to polynucleotides, nucleic acids, proteins, and polypeptides, the term has the same meaning in the present invention. Consequently, because the specification does not teach the detection of carbohydrates and fatty acids, the Examiner finds that the claimed biopolymers are not sufficiently described.

Applicants respectfully disagree. It is well established that inventors are entitled to be their own lexicographer in defining terms to have a specific meaning. *In re Paulsen*, 31 U.S.P.Q. 2d 1671 (Fed.Cir.1994). Applicants limited the meaning of the term "biopolymer" in the present application to nucleic acids, polynucleotides, polypeptides, proteins, and analogs thereof (page 6, lines 18-31). Because the present application provides a specific definition of the term "biopolymer," any other definition of the term, including the one that the Examiner proposes, is of no consequence. Accordingly, applicants respectfully submit that the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

Claims 29-34 and 38-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claims 29-

34 and 38-42 are rejected for its use of the term "direct adsorption." This rejection is respectfully traversed.

Applicants respectfully draw the Examiner's attention to page 8, lines 13-21, of the specification. The specification defines the term "direct adsorption" as an adsorption without any chemical linkers. It is further noted in the specification that "unlike the related art, which uses chemical cross-linking of biopolymers to the substrates, the present invention allows immobilization of both unmodified and modified biopolymers on substrates by simple air-drying on the substrate." Finally, the specification provides a possible theoretical explanation of the term "direct adsorption" as a result of ionic and hydrophobic non covalent interaction between biopolymers and their substrates (page 8, lines 22-28). Accordingly, applicants submit that the specification clearly defines the term "directly attached" as immobilized by adsorption without chemical cross-linking.

Claim 32 is rejected, because it uses the term "analogues thereof." Applicants traverse this rejection.

The term "analogues" is defined by The Random House Webster's Unabridged Dictionary of the English Language (Second Edition, 1997) as a group of chemical compounds similar in structure but different in respect to elemental composition. Accordingly, those skilled in the art will readily recognize that the term "analogues thereof" refers to compounds similar in structure to the ones listed in claim 32, but having different elemental composition. Since "a specification need not describe—and best omits—that which is well-known in the art" (See, e.g., *In re Buchner*, 929 F.2d 660, 661, 18 U.S.P.Q.2d 1331, 1332 (Fed.Cir.1991)), the objected term is not indefinite, because a reasonable amount of guidance is given by the specification so that it would be only a routine matter for one of skill in the art to apply the present invention to analogues of the listed compounds. The objected term is well-defined in both in English language and in the art, broadly used and understood by those skilled in the art, and as such, do not need to be listed in the specification.

In view of the foregoing, it is respectfully submitted that the rejection of claims 29-34 and 38-42 under 35 U.S.C. § 112, second paragraph, should be withdrawn.

Claims 29-34, 38, and 41-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Matson et al. (U.S. Pat. No. 5,981,185). Applicants respectfully traverse this rejection.

The present invention is directed to the immobilization of biopolymers on substrates via direct adsorption. Accordingly, the independent claim 29, which is directed to a method of detecting a target biopolymer, requires a step of contacting either the probe or target biopolymer with a surface of the substrate under a condition sufficient for a direct adsorption.

As explained on page 12, lines 14-25, of the specification, for the purpose of the present invention, a condition is sufficient if it allows the probe or target to adsorb on the substrate. For example, in one embodiment of the present invention, which is described in detail in the Example 1, 10 nl aliquots of cDNA solutions are applied to an aminated polypropylene substrate. Following the application of the cDNA, the substrates are air-dried at 35°C for 15 minutes. Then, the substrates are either soaked in ethanol for one hour or in ammonium hydroxide for 15 minutes to remove loosely bound nucleic acid. Finally, the slides are briefly rinsed with water and air-dried.

It is an unexpected discovery of the present invention that modified substrates, and particularly plasma aminated polypropylene and polysterene substrates are capable of direct and stable adsorption of nucleic acids, proteins, polypeptides, and their analogues without chemical crosslinking (page 3, lines 26-30). As emphasized on page 8, lines 13-21, of the specification, such a "direct adsorption" allows the immobilization of both modified and unmodified biopolymers by simple air-drying without any chemical spacer arms or linkers. Consequently, the present invention provides a number of advantages over the conventional methods. The advantages include, for example, a simplification of the production of biopolymer arrays and a decrease in their manufacturing costs (page 5, lines 25-30).

The Matson reference does not anticipate the present independent claim 29 because it does not teach each element of the claim. In particular, Matson does not teach direct adsorption of biopolymers on substrates. Instead, Matson teaches covalent coupling of biopolymers to supports via spacers or linkers (column 3, lines 60-67, and column 7, lines 10-17). Alternatively, the Matson reference teaches synthesizing biopolymers directly on a surface of a substrate. In this method, a phosphoramidite-activated nucleotide covalently reacts with amine groups on the substrate to form a starting point for oligonucleotide synthesis (column 7, lines 26-33, and column 10, lines 21-39). Therefore, the Matson reference does not teach direct adsorption of biopolymers on a substrate. Accordingly, the Matson reference does not anticipate the instant claim 29.

The Matson reference does not suggest the instant claim 29 and, therefore, cannot make claim 29 obvious. As explained in the Introduction of the present specification, it is generally understood in the art that the immobilization of biopolymers on substrates require either direct covalent interaction between modified substrates and biopolymers or covalent bonding via spacers or linkers. This is exactly the approach undertaken in the Matson reference. Therefore, the Matson reference has no teaching or suggestion that would have motivated one skilled in the art to arrive at the method of the present claim 29. Consequently, the Matson reference does not teach or suggest the present claim 29. Claims 30-34, 38, and 41-42 depend on claim 29, directly or indirectly, and are patentable over the Matson reference for at least the same reasons.

Claims 29-34 and 38-42 are rejected under 35 U.S.C. 102(e) as being anticipated by Rampal (U.S. 6,013,789). This rejection is respectfully traversed.

As explained above, the instant independent claim 29 requires a direct adsorption of a biopolymer on a substrate. Rampal does not anticipate claim 29, because it does not teach each limitation of claim 29. In particular, the Rampal reference does not teach a direct adsorption of a biopolymer on a substrate. On the contrary, the Rampal reference is directed to a covalent attachment of pre-synthesized oligonucleotides to derivatized polypropylene supports (see title,

abstract, column 3, lines 24-57). Therefore, Rampal does not anticipate claim 29 of the present invention.

Rampal does not suggest the instant claim 29. Nothing in Rampal would have motivated one skilled in the art to arrive at the above-described method steps of the present claim 29. Similarly to the Matson reference, the Rampal reference follows the conventional approach to the immobilization of biopolymers on solid substrates by covalent bonding. The attachment method of Rampal requires the presence of a terminal phosphate on the oligonucleotide being attached (column 7, lines 52-55). Then, the covalent attachment of the oligonucleotide to the aminated substrate is accomplished by the formation of a phosphoramidate bond between the oligonucleotide and the substrate (column 8, lines 34-48).

Moreover, Rampal teaches away from the present invention. In the Background of the Invention Section, Rampal emphasizes the weaknesses of the adsorption method as compared to the covalent attachment method (column 2, lines 23-33). In view of that teaching, one skilled in the art would have been discouraged in attempting direct adsorption of biopolymers on substrates. Therefore, base claim 29, as well as dependent claims 30-42 are patentable over the Rampal reference.

The art, made of record but not relied upon by the Examiner, has been considered. However, it is submitted that this art neither describes nor suggests the presently claimed invention.

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles, California telephone number 213-337-6700 to discuss the steps necessary for placing the application in condition for allowance.

Respectfully submitted,

HOGAN & HARTSON L.L.P.

Date: September 21, 2001

By: _____

Wei-Ning Yang
Registration No. 38,690
Attorney for Applicant(s)

500 South Grand Avenue, Suite 1900
Los Angeles, California 90071
Phone: 213-337-6700
Fax: 213-337-6701

Version with markings to show changes made:

IN THE SPECIFICATION:

Please replace the text of the last paragraph on page 12, lines 1-6 with the following text:

polypeptides, proteins, and their analogues. For example, when the target is a polynucleotide, the probe may comprise a polynucleotide that is [complimentary] complementary to the target polynucleotide (see Figure 1). When the target is a receptor or a ligand, the probe may comprise a ligand or a receptor that respectively recognizes and binds to the target receptor or ligand. When the target is an antigen, the probe may comprise an antibody that recognizes the antigen, or vice versa (see Figure 2).

IN THE CLAIMS

Please replace the text of claim 33 with the following text:

33. The method of claim 29, wherein the target biopolymer is a target polynucleotide, and the probe biopolymer is a polynucleotide that is [complimentary] complementary to the target polynucleotide.

Please replace the text of claim 35 with the following text:

35. The method of claim 34, wherein the biopolymer is a polynucleotide, the reporter is biotin, and the method of claim [29] 34 further comprises a step of incubating the complex adsorbed on the surface of the polypropylene substrate with streptavidin-alkaline phosphatase and an ELF reagent for developing a fluorescent signal prior to the detecting step.